

USSN 10/824,244

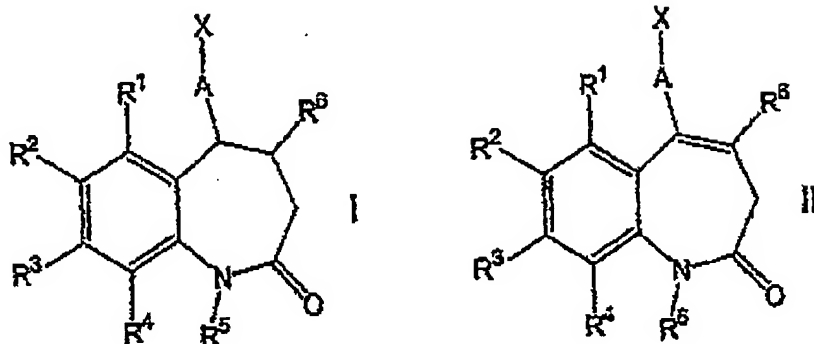
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II. CLAIM AMENDMENTS

1. (Currently Amended) A compound of formulae I or II,



in which

R^1 , R^2 , R^3 and R^4 , identical or different, denote a linear or branched, saturated or unsaturated aliphatic C_{1-10} group or a saturated or unsaturated cycloaliphatic C_{3-7} group, wherein each of the above-stated groups may optionally be bonded via an ether bridge, or hydrogen, a halogen or a hydroxy group,

R^5 denotes hydrogen, a linear or branched, saturated or unsaturated aliphatic C_{1-10} group, or an aryl group,

R^6 denotes hydrogen or a group of the formula $-CH_2-NR^7_2$, wherein the two groups R^7 are identical or different and have the meaning stated below or may form a 3-8-membered ring together with the nitrogen atom connecting them as a ring member,

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R⁷ denotes a linear or branched, saturated or unsaturated aliphatic C₁₋₆ group or a saturated or unsaturated cycloaliphatic C₃₋₆ group,

A denotes a bridge with one of the following formulae:

$-(CH_2)_{n+2}-$, $-(CH_2)_n-CH=CH-$, $-(CH_2)_nCOO-$, $-(CH_2)_nCONH-$, $-(CH_2)_{n+1}O(CH_2)_pCO-$, $-(CH_2)_{n+1}O-$, $-(CH_2)_{n+1}NR^{1'}-$ in which n denotes 0, 1, 2, or 3, and p denotes 0 or 1, R¹ has the meaning stated hereinafter and the bond to the group X is always stated last,

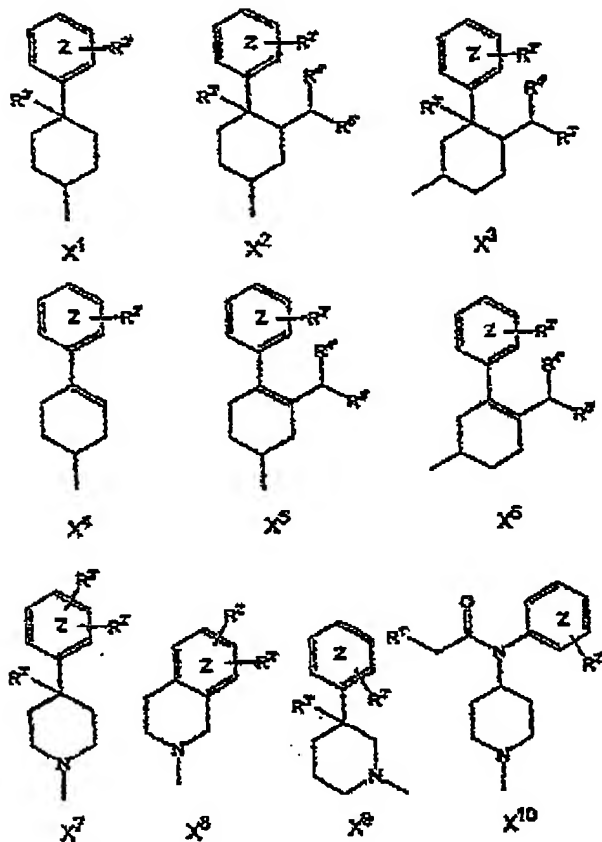
and X denotes one of the following groups of the general formulae X¹ to X⁶ and X¹⁶, in which the unoccupied bond line symbolises the bond to the bridge A and

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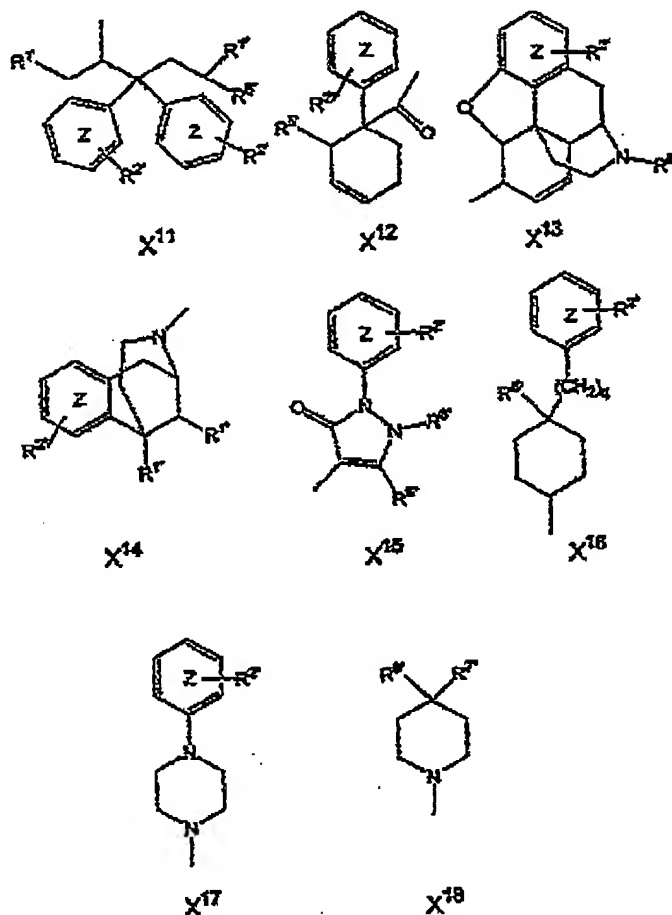


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in which

R¹ denotes hydrogen, a linear or branched, saturated or unsaturated aliphatic C₁₋₁₀ group, a saturated or unsaturated cycloaliphatic C₃₋₇ group, or an aryl group,

R² denotes a linear or branched, saturated or unsaturated aliphatic C₁₋₁₀ group, a saturated or unsaturated cycloaliphatic C₃₋₇ group or an aryl group

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wherein all above-stated groups may optionally be joined via an ether, thioether or SO₂ bridge, or hydrogen, a halogen, a hydroxy, thiol, cyano or nitro group or a group of the formula -NR^{1'}₂ wherein the two groups R^{1'} are identical or different and have the above-stated meaning,

R^{3'} denotes a linear or branched, saturated or unsaturated aliphatic C₁₋₁₀ group, a saturated or unsaturated cycloaliphatic C₃₋₇ group, or an aryl group, wherein all the above-stated group may optionally be joined via an ether or an ester bridge, hydrogen, a halogen, a hydroxy group,

R^{4'} denotes hydrogen, or an aryl group, wherein the aryl group may comprise at least one substituent R^{2'} with the above meaning, with the exception of hydrogen,

R^{5'} denotes a of the formula -NR^{6'}₂, wherein the two R^{6'} may be identical or different and have the meaning stated hereinafter or may form a 3-7-membered ring together with the nitrogen atom connecting them as a ring member, which ring may optionally contain at least one oxygen and/or at least one further nitrogen as a ring atom, wherein the nitrogen may comprise a substituent R^{10'} with the meaning stated hereinafter,

R^{6'} denotes a linear or branched, saturated or unsaturated aliphatic C₁₋₆ group, a saturated or unsaturated or cycloaliphatic C₃₋₇ group, or an aryl group,

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R⁹ denotes hydrogen, a linear or branched aliphatic C₁₋₁₀ residue,

R¹⁰ denotes hydrogen, a linear or branched, saturated or unsaturated aliphatic C₁₋₁₀ group, or an aryl group and

Z denotes at least one optionally present nitrogen as a ring atom,

and q denotes 0, 1, 2 or 3,

optionally in the form of the racemates thereof, the pure stereoisomers thereof, or in the form of mixtures of the stereoisomers, in any desired mixing ratio or in each case in the form of the acids or bases thereof or in the form of the salts thereof, ~~or in the form of the solvates thereof.~~

2. (Currently Amended) A compound according to claim 1, characterised in that R² and R³, identical or different, denote a linear or branched, saturated or unsaturated aliphatic C₁₋₃ residue group or a halogen and R¹ and R₄ in each case denote hydrogen, R⁵ denotes hydrogen or a linear or branched, saturated or unsaturated aliphatic C₁₋₃ group and R⁶ denotes hydrogen or a group of the formula -CH₂-NR⁷₂, in which R⁷ denotes a linear or branched, saturated or unsaturated aliphatic C₁₋₃ group, optionally in the form of the racemates thereof, the pure stereoisomers thereof, ~~in particular enantiomers or diastereomers,~~ or in the form of mixtures of the stereoisomers, ~~in particular the enantiomers or diastereomers,~~ in any desired

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mixing ratio or in each case in the form of the acids or bases thereof or in the form of the salts thereof, ~~in particular physiologically acceptable salts, or in the form of the solvates thereof, in particular hydrates.~~

3. (Currently Amended) Substituted benzo[b]azepin-2-one compounds and in each case the tautomers thereof A compound according to claim 1, characterised in that R² and R³ in each case denote a methyl group or a chlorine and R¹ and R⁴ in each case denote hydrogen, R⁵ denotes hydrogen or a methyl group and R⁶ denotes hydrogen or a group residue of the formula - CH₂-N(CH₃)₂, optionally in the form of the racemates thereof, the pure stereoisomers thereof or in the form of mixtures of the stereoisomers, in any desired mixing ratio or in each case in the form of the acids or bases thereof or in the form of the salts thereof ~~or in the form of the solvates thereof.~~

4. (Currently Amended) A compound according to claim 1, characterized in that R³ denotes a linear or branched, saturated or unsaturated aliphatic C₁₋₃ group or a halogen and R¹, R² and R⁴ in each case denote hydrogen, R⁵ denotes hydrogen or a linear or branched, saturated or unsaturated aliphatic c₁₋₃ group and R⁶ denotes hydrogen or a group of the formula -CH₂-N(R⁷)₂, in which R⁷ denotes a linear or branched, saturated or unsaturated aliphatic c₁₋₃ group, optionally in the form of the racemates thereof, the pure stereoisomers thereof or in the form of mixtures of the stereoisomers, in any desired mixing ratio or in each case in the form of the acids or bases thereof or in the form of the salts thereof, ~~or in the form of the solvates thereof.~~

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5. (Currently Amended) A compound according to claim 1, characterised in that R^3 denotes a methyl group or a chlorine and R^1 , R^2 and R^4 in each case denote hydrogen, R^5 denotes hydrogen or a methyl group and R^6 denotes hydrogen or a of the formula $-CH_2-N(CH_3)_2$, optionally in the form of the racemates thereof, the pure stereoisomers thereof, or in the form of mixtures of the stereoisomers, in any desired mixing ratio or in each case in the form of the acids or bases thereof or in the form of the salts thereof, ~~or in the form of the solvates thereof.~~

6. (Currently Amended) ~~Substituted benzo[b]azepin-2-one compounds and in each case the tautomers thereof~~ A compound according to claim 1, characterised in that R^1 and R^3 , identical or different, denote a linear or branched, saturated or unsaturated aliphatic C_{1-3} group or a halogen and R^2 and R^4 in each case denote hydrogen, R^5 denotes hydrogen or a linear or branched, saturated or unsaturated aliphatic C_{1-3} group and R^6 denotes hydrogen or a group of the formula $-CH_2-NR^7_2$, in which R^7 denotes a linear or branched, saturated or is unsaturated aliphatic C_{1-3} group, optionally in the form of the racemates thereof, the pure stereoisomers thereof, or in the form of mixtures of the stereoisomers, in any desired mixing ratio or in each case in the form of the acids or bases thereof or in the form of the salts thereof, ~~or in the form of the solvates thereof.~~

7. (Currently Amended) A compound according to claim 1, characterised in that R^1 and R^3 in each case denote a methyl group or a chlorine and R^2 and R^4 in each case denote hydrogen, R^5

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denotes hydrogen or a methyl group and R^6 denotes hydrogen or a of the formula $-\text{CH}_2-\text{N}(\text{CH}_3)_2$, optionally in the form of the racemates thereof, the pure stereoisomers thereof, or in the form of mixtures of the stereoisomers, in any desired mixing ratio or in each case in the form of the acids or bases thereof or in the form of the salts thereof, ~~or in the form of the solvates thereof.~~

8. (Currently Amended) A compound according to claim 1, characterised in that A denotes a bridge of the formula $-\text{CH}_2-\text{COO}-$ or $-\text{CH}_2\text{CONH}-$ optionally in form of the racemates thereof, the pure stereoisomers thereof, in particular enantiomers or diastereomers, or in the form of mixtures of the stereoisomers, in any desired mixing ratio or in each case in the form of the acids or bases thereof or in the form of the salts thereof, ~~or in the form of the solvates thereof.~~

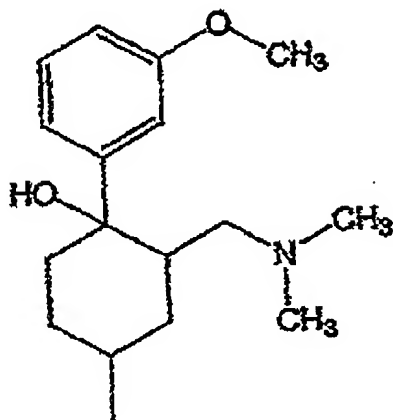
9. (Currently Amended) A compound according to claim 1, characterised in that X denotes a group of the following formula:

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optionally in the form of the racemates thereof, the pure stereoisomers thereof or in the form of mixtures of the stereoisomers, in any desired mixing ratio or in each case in the form of the acids or bases thereof or in the form of the salts thereof, ~~or in the form of the solvates thereof.~~

10. (Currently Amended) A compound according to claim 1 which is:

2'-(8-Chloro-2-oxo-2,3-dihydro-1H-benzo[b]azepin-5-yl)acetic acid [3''-(N,N-dimethylaminomethyl)-4''-hydroxy-4''-(m-methoxyphenyl)cyclohexyl] ester,

2'-(8-Chloro-1-methyl-2-oxo-2,3-dihydro-1H-benzo[b]azepin-5-yl)acetic acid [3''-(N,N-dimethylaminomethyl)-4''-hydroxy-4''-(m-methoxyphenyl)cyclohexyl] ester,

2'-(8-Chloro-2-oxo-2,3-dihydro-1H-benzo[b]azepin-5-yl)-N-[3''-N,N-dimethylaminomethyl)-4''-hydroxy-4''-(m-

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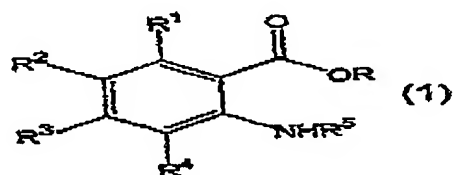
methoxyphenyl)cyclohexyl]acetamide,

2'-(8-Chloro-1methyl-2-oxo-2,3-dihydro-1H-benzo[b]azepin-5-yl)-
N-[3''-(N,N-dimethylaminomethyl)-4''-hydroxy-4''-(m
methoxyphenyl)cyclohexyl]acetamide,

optionally in the form of the racemates thereof, the pure stereoisomers thereof, or in the form of mixtures of the stereoisomers, in any desired mixing ratio or in each case in the form of the acids or bases thereof or in the form of the salts thereof, ~~or in the form of the solvates thereof.~~

11. (Currently Amended) A process for the production of a compound according to claim 1, characterised in that

A) an optionally substituted 2-aminobenzoic alkyl ester of the formula (1), in which R¹, R², R³, R⁴ and R⁵ have the same meaning as in claim 1 and R denotes an alkyl group,



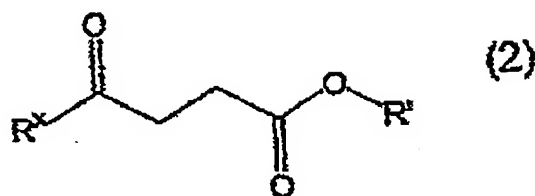
is reacted with succinic acid dialkyl ester of the ~~general~~ formula (2), in which R' denotes an alkyl group and R^x denotes chlorine or an alkoxy group,

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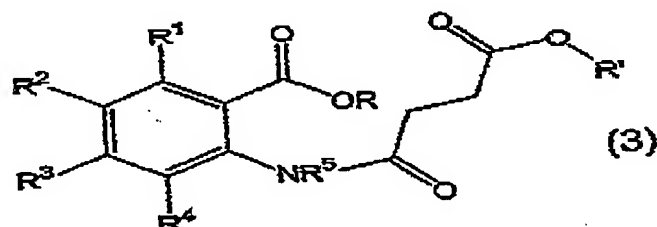
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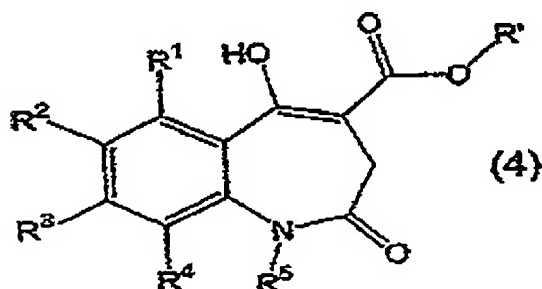
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under suitable reaction conditions, in a suitable solvent, and is then worked up, optionally followed by purification of the optionally substituted N- (2-carbalkoxyphenyl)succinic acid alkyl ester amide formed of the formula (3), in which R, R', R¹, R², R³, R⁴ and R⁵ have the above-stated meaning



B) an optionally substituted N-(2-carboalkoxyphenyl)succinic acid alkyl ester amide of the formula (3) is reacted in the presence of potassium tert-butanolate in a suitable solvent and



then worked up, optionally followed by purification of the optionally substituted 5-hydroxy-2-oxo-2,3-dihydro-1H-benzo[b]azepin-4-carboxylic acid alkyl ester formed of the

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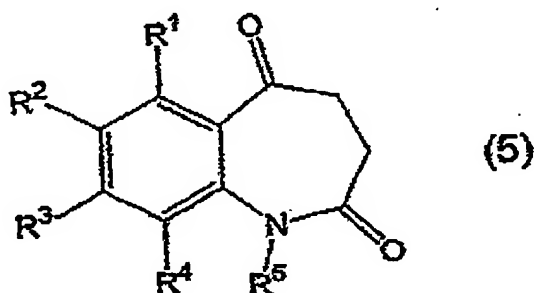
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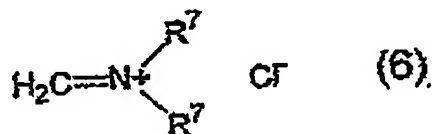
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general formula (4), in which R' , R^1 , R^2 , R^3 , R^4 and R^5 have the above-stated meaning,

C) an optionally substituted 5-hydroxy-2-oxo-2,3-dihydro-1H-benzo[b]azepin-4-carboxylic acid alkyl ester of the general formula (4) is reacted in a dimethyl sulfoxide/Water mixture at elevated temperature and then worked up, optionally followed by purification of the optionally substituted 2,3,4, 5-tetrahydro-1H-benzo[b]azepin-2,5-dione of the general formula (5), in which R' , R^2 , R^3 , R^4 and R^5 have the above-stated meaning,



D) an optionally substituted 2,3,4,5-tetrahydro-1H-benzo[b]azepin-2,5-dione of the formula (5) is reacted with a substituted aminomethyl hydrochloride of the formula (6), in which the group R^7 has the meaning stated in claim 1,



in the presence of an acid, in a suitable solvent, and then worked up, optionally followed by purification of the optionally

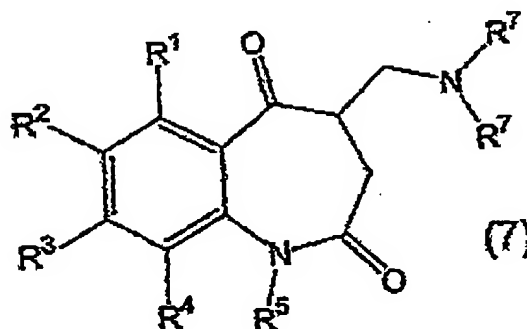
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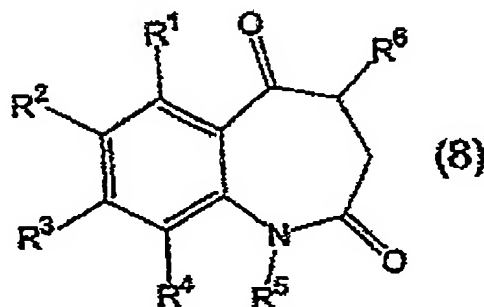
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substituted aminomethyl-2,3,4,5-tetrahydro-1H-benzo[b]azepin-2,5-dione of the ~~general~~ formula (7), in which R^1 , R^2 , R^3 , R^4 , R^5 and R^7 have the above-stated meaning,



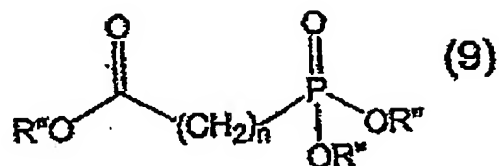
- E) an optionally substituted 2,3,4,5-tetrahydro-1H-benzo[b]azepin-2,5-dione of the formula (8), in which R^1 , R^2 , R^3 , R^4 , R^5 and R^6 have the same meaning as in claim 1 and which combines the compounds of the formulae (5) and (7)



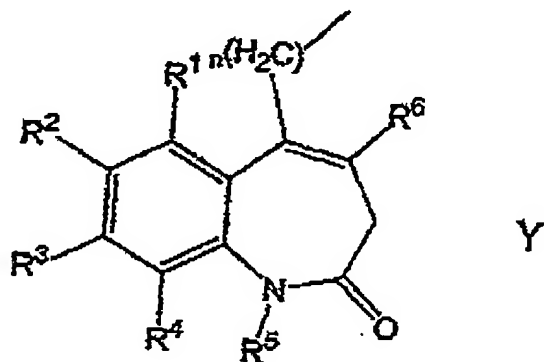
is reacted with a phosphonoalkanoic acid trialkyl ester of the ~~general~~ formula (9), in which n has the same meaning as in claim

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1 and R'' denotes an alkyl group,



in the presence of a base, in a suitable solvent, and then worked up, optionally followed by Purification of the compound formed of the formula Y-COOR'' in which R'' has the above stated meaning and Y denotes a group of the formula Y, in which the unoccupied bond line symbolises the bond to the group -COOR'' and



in which R', R², R³, R⁴, R⁵, R⁶ and n have the above-stated meaning.

F) optionally an ester of the formula Y-COOR'' is reacted in the presence of a base, in a suitable solvent, and then worked up, optionally followed by Purification of the carboxylic acid formed of the formula Y-COOH in which Y has the above-

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stated meaning,

G) optionally a carboxylic acid of the formula $Y-COOH$ or a carboxylic acid ester of the formula $Y-COOR''$ in which Y and R'' have the above stated meaning, is derivatised in that

a) a carboxylic acid or carboxylic acid ester of the formula $Y-COOH$ or $Y-COOR''$ is reduced with the assistance of reducing agents, preferably lithium aluminium hydride, in a suitable solvent, preferably tetrahydrofuran, to the corresponding alcohol of the formula $Y-CH_2-OH$,

b) a carboxylic acid or carboxylic acid ester of the formula $Y-COOH$ or $Y-COOR''$ is reduced with the assistance of reducing agents, in a suitable solvent, to the corresponding aldehyde of the formula $Y-CHO$ or

c) an alcohol of the formula $Y-CH_2-OH$ according to a) is reacted with a brominating agent, to yield the corresponding bromide of the formula $Y-CH_2-Br$ and then worked up and the product is optionally purified,

H) a compound of the formula X^I-R^{IV} , in which X^I has the above-stated meaning and R^{IV} denotes a functional group, is optionally produced in that

a) 1,4-cyclohexanedione monoethylene ketal, 4-oxocyclohexan-1-one ethylene ketal or 4-oxocyclohexane carboxylic acid is reacted with magnesium and a brominated

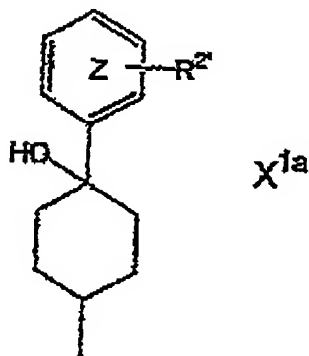
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or chlorinated, optionally substituted aromatic or heteroaromatic compound in a suitable solvent, at elevated temperature to yield the corresponding coupling product and then the ketal is optionally cleaved by reaction with hydrochloric acid in a suitable solvent, and worked up, optionally followed by purification of the product of the formula $X^{1a}=O$, $X^{1a}-NHR^1$ or $X^{1a}-CO_2H$, in which X^{1a} denotes a group of the formula X^{1a} and R^1 , R^2 and Z have the above-stated meaning and the unoccupied bond line symbolises the



bond to the group $=O$, $-NHR^1$ or $-CO_2H$,

b) Optionally a ketone of the formula $X^{1a}=O$ is reacted in the presence of a suitable reducing agent, in a suitable solvent, to yield the corresponding alcohol of the formula $X^{1a}-OH$, worked up and the product is optionally purified,

c) Optionally a ketone of the formula $X^{1a}=O$ is reacted under nitrogen in a suitable solvent, firstly with ammonium trifluoroacetate and then with glacial acetic acid and sodium triacetoxy borohydride, to yield the corresponding amine of the formula $X^{1a}-NH_2$, worked up and the product is optionally purified,

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d) optionally a carboxylic acid of the formula $X^{1a}=CO_2H$ is activated by reaction with dicyclohexylcarbodiimide or by conversion into the carboxylic acid chloride or a mixed anhydride, reacted with diazomethane in a suitable solvent, and then treated with water, worked up and the product of the formula $X^{2-}-CO-CH_2-OH$ is optionally purified,

e) optionally the hydroxy group in position 4 of the cyclohexane ring in the group X^{1a} is converted into hydrogen, a halogen, an ether, ester, alkyl, or aryl group, in that

α) in order to introduce an ether group, a compound from one of steps a) -d) is reacted with an aliphatic or cycloaliphatic compound in the presence of a suitable catalyst in a suitable solvent, or with an alkylating agent in a suitable solvent, or with an aryl compound in the presence of diethylazo dicarboxylate and triphenylphosphine,

β) in order to introduce a halogen, a compound from one of steps a) -d) is reacted with a halogenating agent in a suitable solvent, preferably with $POCl_3$ in dimethylformamide, with PPh_3/Cl_2 , with PPh_3/Br_2 , with triphenylphosphine/n-chlorosuccinimide or with $HCl/ZnCl_2$,

γ) in order to introduce a hydrogen, a compound from step β) is reacted with hydrogen in the presence of a suitable catalyst, in a suitable solvent,

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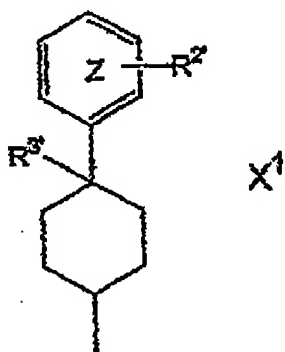
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δ) in order to introduce an aliphatic or cycloaliphatic or an aryl group, a compound from step β) is reacted with an aliphatic or cycloaliphatic boronic acid or a boronic acid ester or an aryl or heteroaryl borodihydroxide compound in the presence of palladium(II) acetate and potassium carbonate in a suitable solvent, or

ε) in order to introduce an ester group, a compound from one of steps a) -d) is reacted with a carboxylic acid chloride in the presence of a suitable catalyst in a suitable solvent

and then worked up, optionally followed by purification of the compound formed of the formula X^1-R^{IV} , in which X^1 denotes the



formula X^1

and R^{IV} , $R^{2'}$ and $R^{3'}$ have the above-stated meaning,

I) a compound of the formula $X-R^{IV}$, in which X has the above-stated meaning and R^{IV} denotes a functional group, is optionally

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derivatised in that

a) a ketone of the formula $X=O$ is reacted 1) with methoxymethyl triphenylphosphonium chloride under protective gas in a suitable solvent, preferably in dimethylformamide, in the presence of sodium hydride and then with hydrochloric acid or 2) with $Me_3S \cdot BF_4$ to yield the corresponding aldehyde $X-CHO$ extended by one carbon atom,

b) an aldehyde of the formula $X-CHO$ according to a) is reacted with a reducing agent, preferably sodium borohydride, in a suitable solvent, to yield the corresponding alcohol $X-CH_2-OH$,

c) an alcohol $X-CH_2-OH$ according to b) or of the formula $X-OH$ is reacted with a brominating agent, in a suitable solvent, preferably acetonitrile, to yield the corresponding bromide of the formula XCH_2-Br or $X-Br$,

d) a bromide of the formula $X-CH_2-Br$ according to c) is reacted with a phosphine of the formula PR^V_3 , in which R^V denotes an organic group, in a suitable solvent, preferably toluene, ether, tetrahydrofuran or acetone, with cooling and under protective gas to yield the corresponding phosphonium salt $R^V_3P^+-CHX$ or

e) a bromide of the formula $X-CH_2-Br$ according to c) is reacted with a phosphite of the formula $HP(O)(OR^{VI})_2$, in which R^{VI} denotes an organic group, at elevated temperature, preferably $200^\circ C$, to yield the corresponding phosphonate $(R^{VI}O)_2P(O)-CH_2-X$

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and then worked up and the product is optionally purified,

J) a compound from step F) or G), in which Y has the above-stated meaning, is reacted with a compound of the formula X^1-R^{IV} from step H) or a compound $X-R^{IV}$ from step I), in which X, X^1 and R^{IV} have the above-stated meaning, in that

a) a carboxylic acid of the formula $Y-COOH$ is reacted with an amine of the formula $X-NH_2$ in the presence of a suitable condensing agent, 1-hydroxybenzotriazole and N-methylmorphine, in a suitable solvent, with formation of an amide bridge,

b) a carboxylic acid of the formula $Y-COOH$ is reacted with an alcohol of the formula $X-OH$ in the presence of a suitable condensing agent in a suitable solvent with formation of an ester bridge, the reaction preferably taking place in the presence of methylimidazole and 1-(mesitylene-2'-sulfonyl)-3-nitro-1,2,4-triazole in tetrahydrofuran or in the presence of dicyclohexylcarbodiimide, 1-hydroxybenzotriazole and N-methylmorphine in dimethylformide,

c) a bromide of the formula $Y-CH_2-Br$ is reacted with a compound of the formula $X-CO(CH_2)_p-OH$, in which p has the above-stated meaning, under protective gas in the presence of a suitable catalyst, in a suitable solvent, with formation of a bridge of the formula $-CO(CH_2)_p-O-CH_2$,

d) an alcohol of the formula $Y-CH_2-OH$ is reacted with a

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bromide of the formula X-Br under protective gas in the presence of a suitable condensing agent, in a suitable solvent, preferably dimethylformamide, with formation of an ether bridge,

e) a bromide of the formula Y-CH₂-Br is reacted with an alcohol of the formula X-OH under protective gas in the presence of a suitable condensing agent, in a suitable solvent, preferably dimethylformamide, with formation of an ether bridge,

f) an aldehyde of the formula Y-CHO is reacted with an amine of the formula X-NHR¹ in the presence of a suitable reducing agent, in a suitable solvent, preferably a mixture of tetrahydrofuran and 1,2-dichloroethane, with formation of an amino bridge,

g) an aldehyde of the formula Y-CHO is reacted with a phosphonium salt R''₃P⁺-CHX⁻, in which R'' has the above-stated meaning, under protective gas in the presence of suitable catalysts in a suitable solvent, preferably in the presence of sodium methanolate in a mixture of hexane, diethyl ether and/or diisopropyl ether or in the presence of sodium hydride, potassium tert-butyrate or a lithium amide in dimethylformamide or dimethyl sulfoxide, with formation of a -CH=CH- bridge or

h) an aldehyde of the formula Y-CHO is reacted with a phosphonate of the formula (R'''O)₂P(O)-CH₂-X, in which R''' has the above-stated meaning, under protective gas in the

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presence of suitable catalysts, preferably sodium methanolate, sodium hydroxide, potassium hydroxide, sodium hydride, potassium tert-butyrate or a lithium amide, in a suitable solvent, preferably dimethylformamide, dimethyl sulfoxide, diethyl ether, tetrahydrofuran, with formation of a $-CH=CH-$ bridge and

i) optionally the $-CH=CH-$ bridge from step g) or h) is hydrogenated by hydrogen, preferably at standard pressure or elevated pressure of up to 100 bar, in the presence of suitable catalysts, preferably transition metals or transition metal compounds, preferably palladium or the salts thereof, rhodium or the complexes thereof, in a suitable solvent, preferably dimethylformamide, methanol or ethanol, at a temperature of between 20 and 100°C with formation of a $-CH_2-CH_2-$ bridge and then worked up and the product is optionally purified,

K) optionally the double bond in the 7-membered ring of one of the reaction products from step I) is hydrogenated by hydrogen, preferably at standard pressure or elevated pressure of up to 100 bar, in the presence of suitable catalysts, preferably transition metals or transition metal compounds, preferably palladium or the salts thereof, rhodium or the complexes thereof, in a suitable solvent, preferably dimethylformamide, methanol or ethanol, at a temperature of between 20 and 100°C and then worked up and the product is optionally purified.

12. (Currently Amended) A pharmaceutical preparation containing

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at least one compound of claim 1 and ~~optionally~~ physiologically acceptable auxiliary substances.

13. (Previously Presented) A method of treating pain in a patient in need thereof comprising administering to the patient an effective amount of the pharmaceutical preparation according to claim 12.

14. (Previously Presented) The method according to claim 13 where the pain is selected from chronic pain or neuropathic pain.

15-40. (Cancelled).

41. (Currently Amended) A compound of claim 1 wherein the compound is in the form of enantiomers or diastereomers, mixtures of the enantiomers or diastereomers, physiologically acceptable salts, ~~or in the form of hydrates.~~